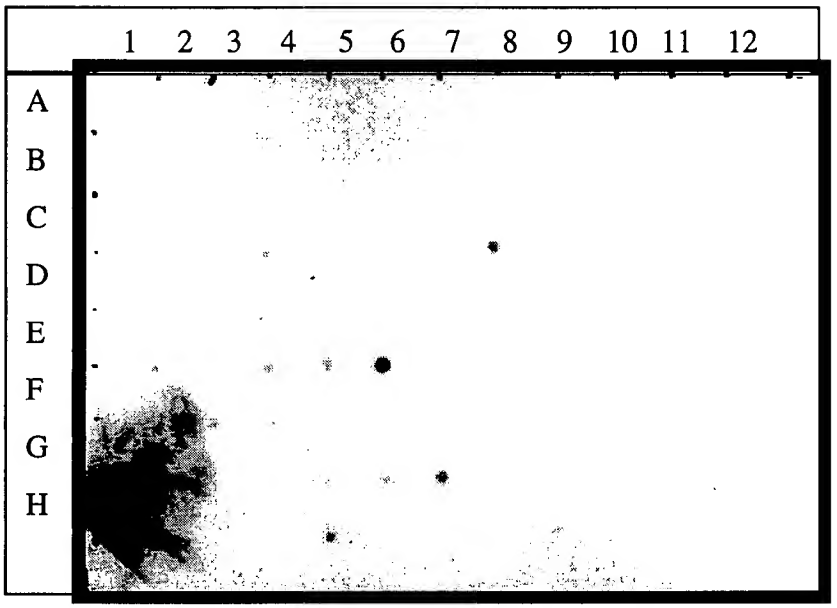
MoAb-based therapy of Cancer: CD38 expression in normal human tissues



Legend: Master blot from Clontech was hybridized with radiolabled human CD38-specific nucleic acid probe. Only the thymus tsisue (from adult and fetal) showed mRNA transcript for CD38. Prostate was also positive but to a lesser extent.

Figure 1

MoAb-based therapy of Cancer: Reversal effect of unconjugated anti-CD38 moAb on IT-induced cytotoxicity in HL-60 cells

Legend: HL-60 cells were incubated With IT alone (C) or IT+RA (5nM) In presence or absence of increasing Concentrations unconjugated anti-CD38 moAb. Cell viability was Tested fter 3 days incubation by using MTS assay

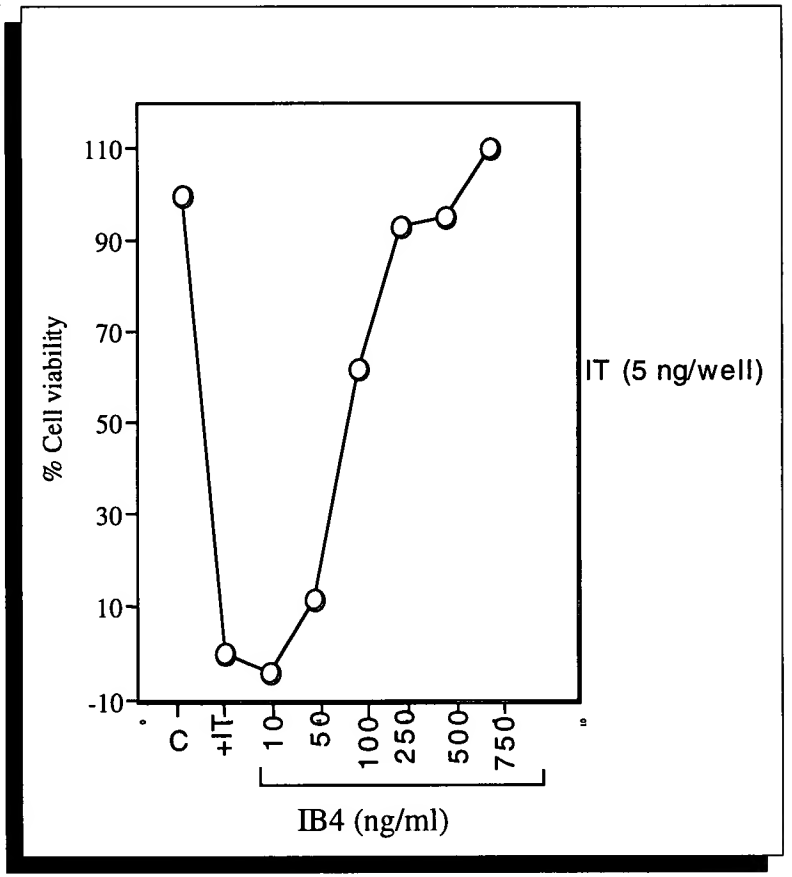


Figure 2

Effect of RA-preteatment on IT-induced killing of HL-60 cells

Legend: HL-60 were incubated with or without RA (5 nM) overnight, wahsed twice and then recultured in The esence or absence of IT alone or In presence of 100-fold excess of nconjugated anti-CD38 moAb. After 3 days incubation cell viability Was termined using MTS assay

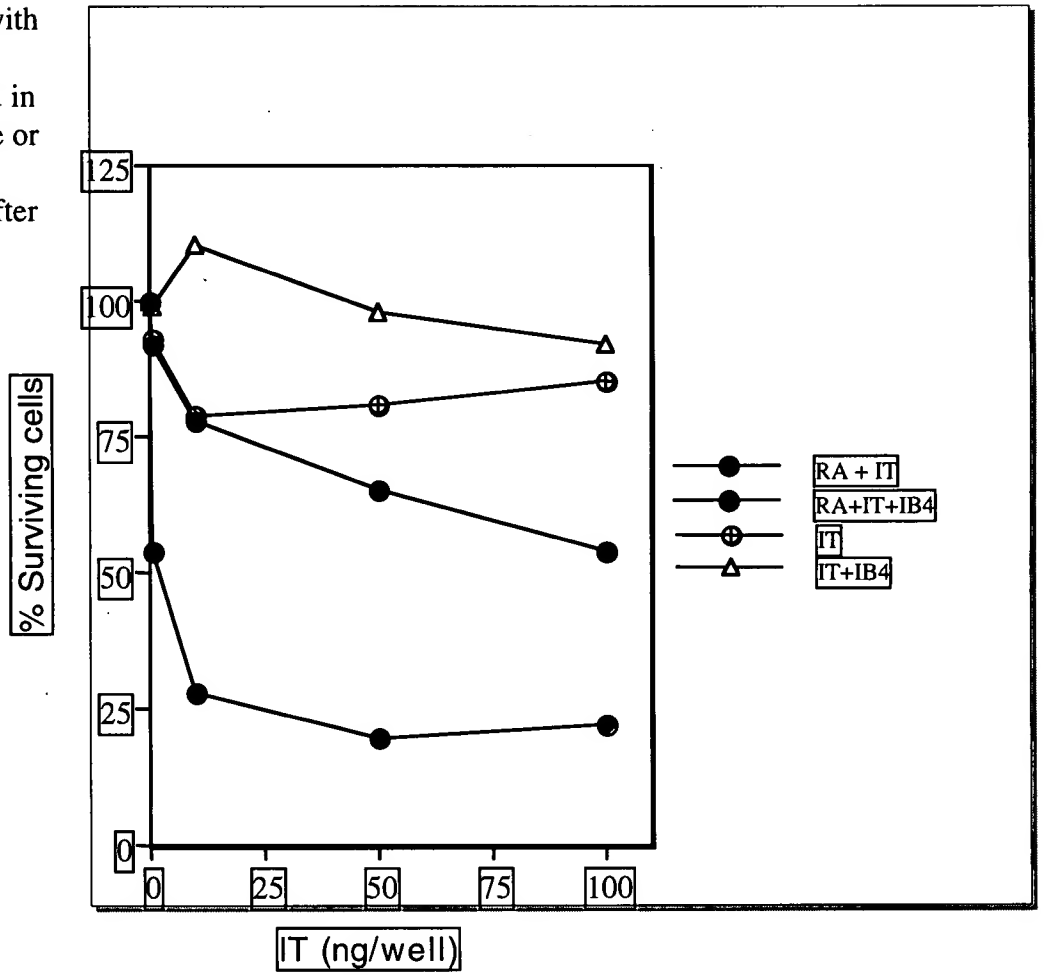


Figure 3

MoAb-based therapy of Cancer:

IB4-gelonin-induced killing of HL-60 cells in presence of RA

Legend: HL-60 cells were incubated For 3 days in presence of IT or gelonin Alone or in presence of 5 nM RA. Cell viability was cheched by MTS assay.

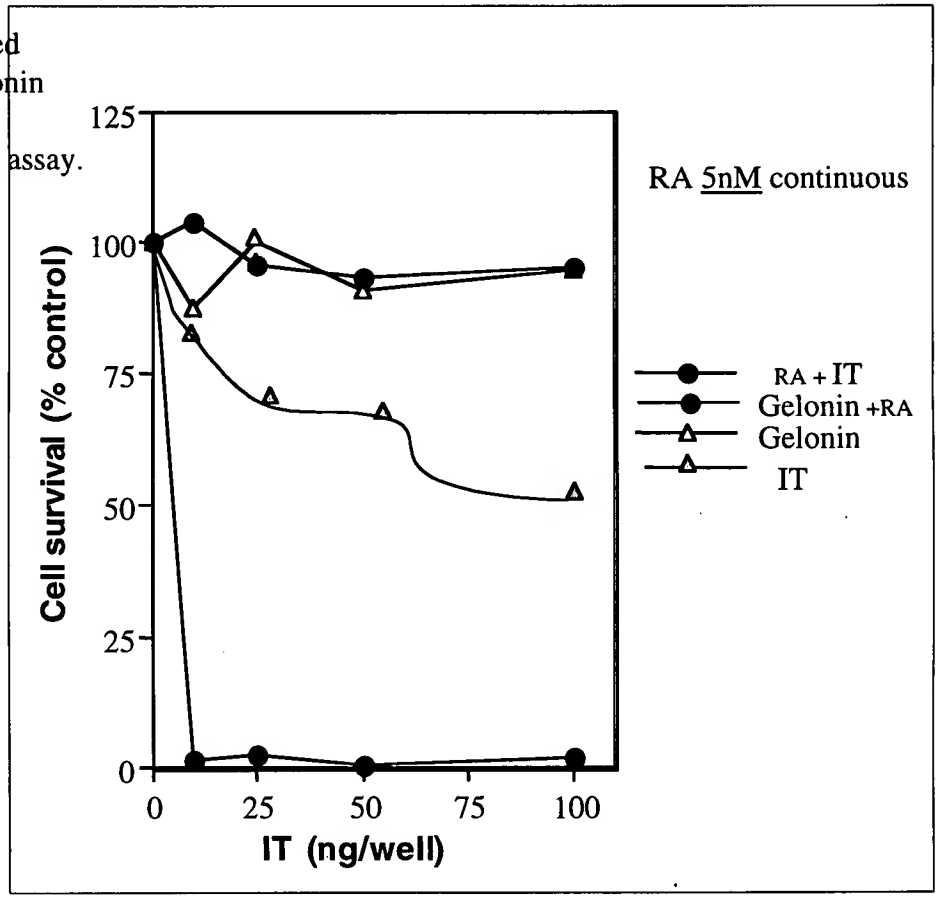


Figure 4

MoAb-based therapy of Cancer:

Effect of increasing RA conc.

Legend: HL-60 were cultured in presence Of IT or unconjugated anti-CD38 moAb Alone the presence of increasing amounts of RA For 3 days. At the end of incubation, cell viability Was dtermined by MTS assay

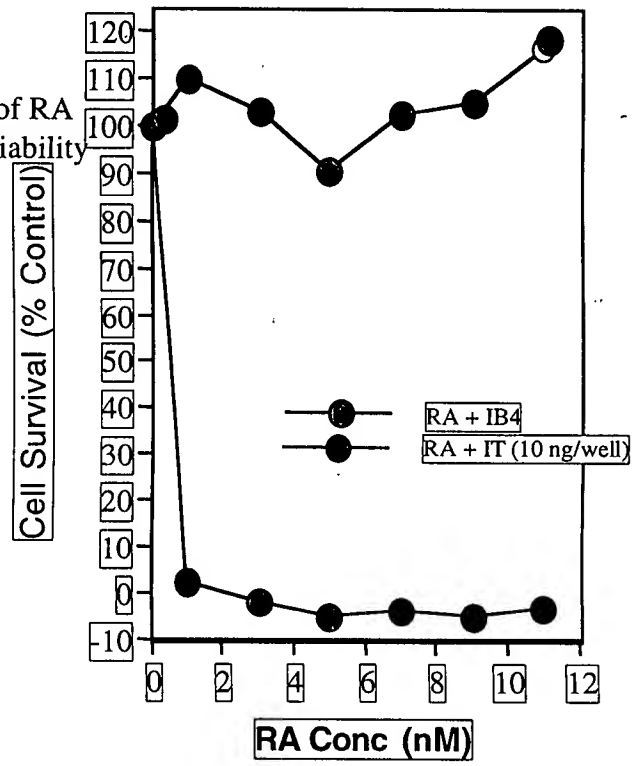
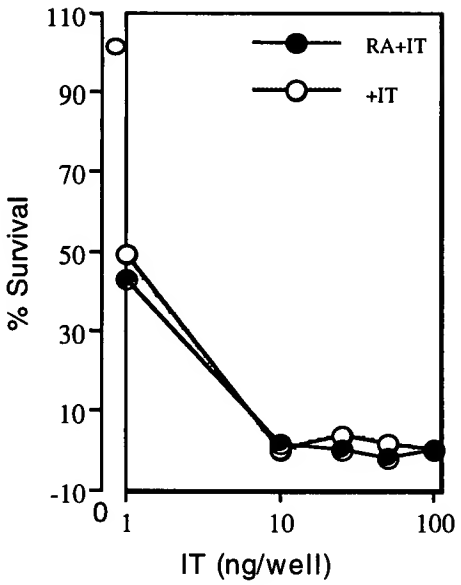
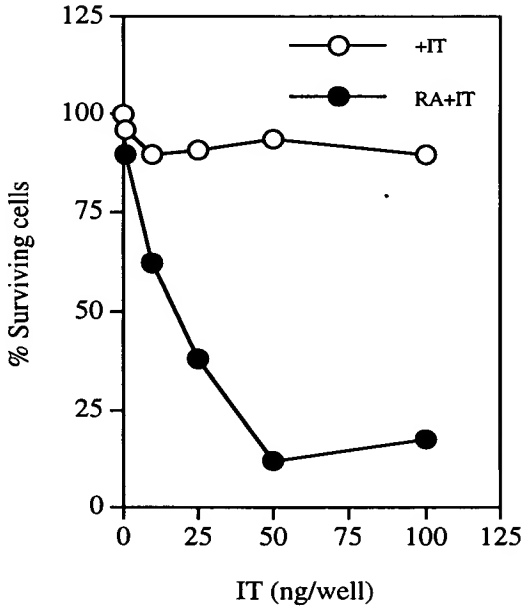


Figure 5

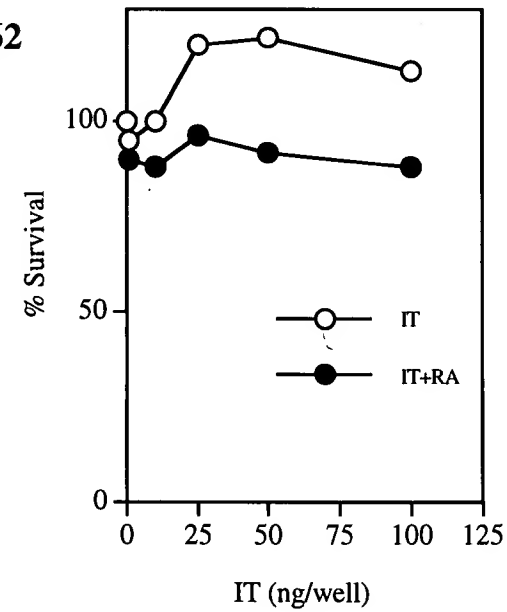
Daudi



THP-1



K562



HL60-RARα

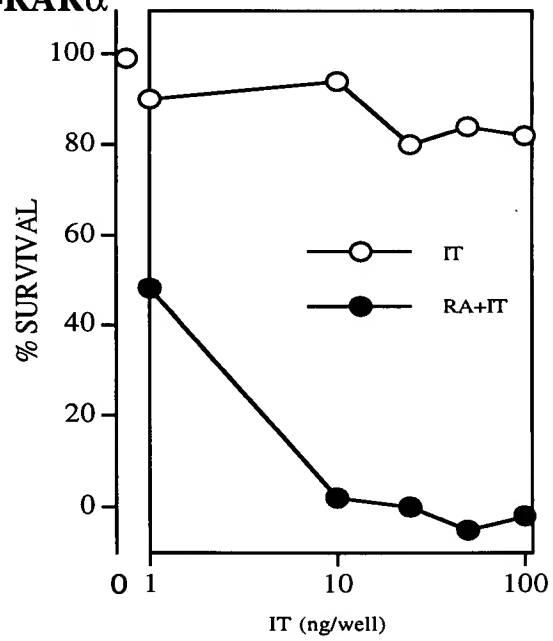


Figure 6

MoAb-based therapy of Cancer:

IT-induced killing of Doxo-resistant HL-60 cells

Legend: HL-60 subcloned cells, resistant to Adriamycin-induced killing were cultured With IT alone in the presence of 5 nM RA. After 3 days incubation, cells viability was tested using MTS assay.

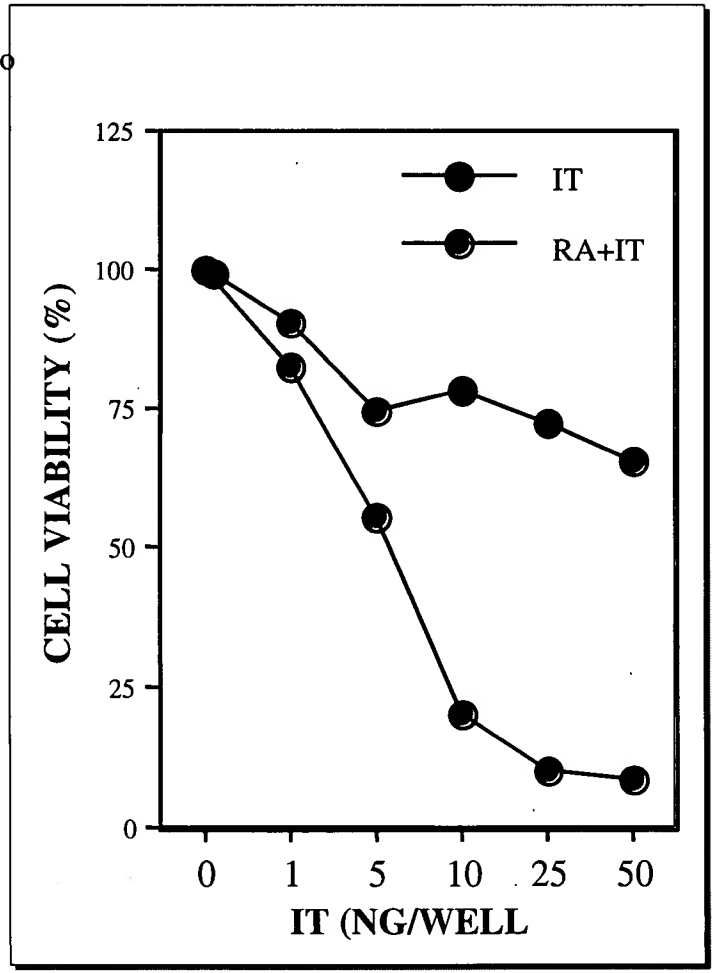


Figure 7

MoAb-based therapy of Cancer:

IT-mediated killing of MZ (NHL) cells

Legend: A non-Hodgkin lymphoma cell line that has a high basal expression of CD38 antigen was incubated with IT in presence or absence of RA. The cell cell viability was checked after 3 days culture using MTS assay.

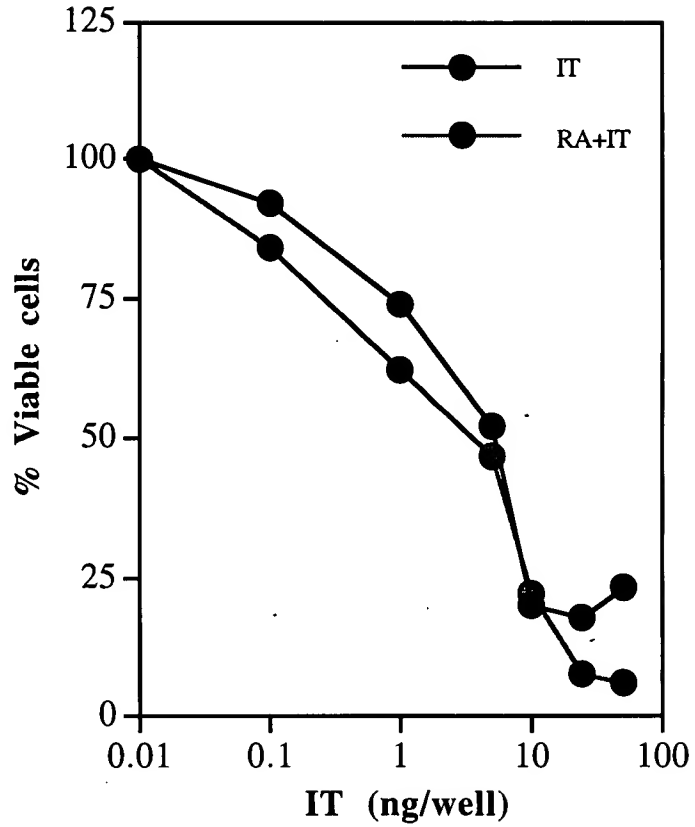


Figure 8

Legend: An HL-60 subclone with mutated RARalpha genethat renders these cells resistant to RA-induced CD38 expression, was cultured with IT alone or in presence of 5 mM RA. After 3 days the cell viability was determined using MTS assay.

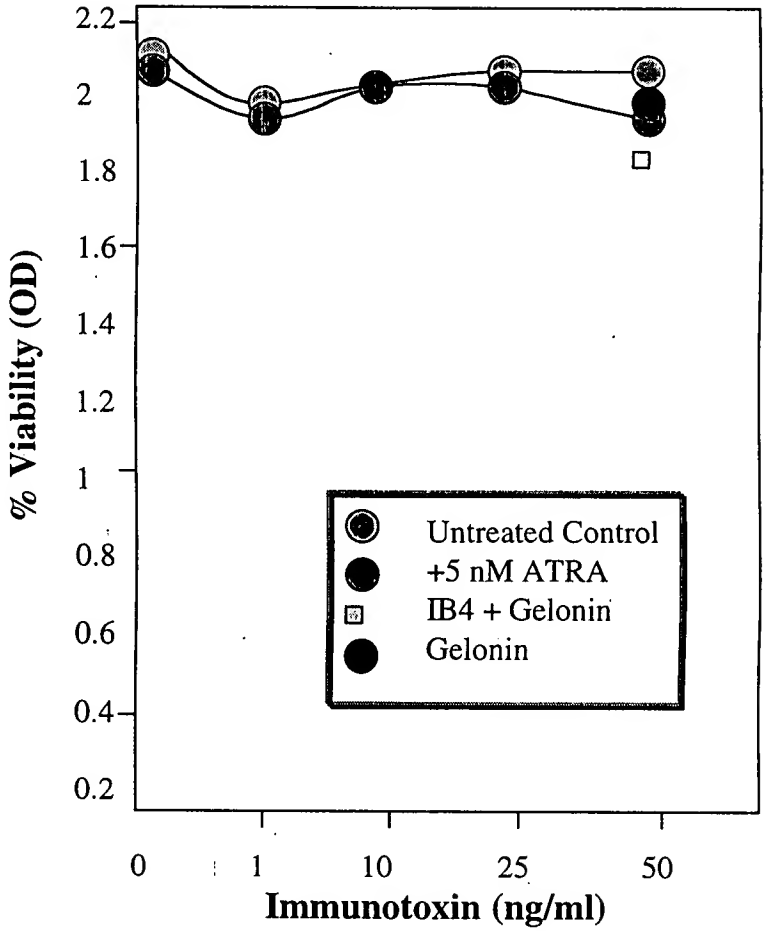


Figure 9

Potential targets for anti-CD38 bound toxin treatment

Cell target	Basal CD38	CD38 after RA treatment
AML	50 ± 10	180 ± 20
APL	6 ± 4	120 ± 30
Lymphomas	80 ± 20	210 ± 10
Myelomas	60 ± 20	180 ± 25
SLE	B cells producing self reactive ab	
Myesthenia gravis		
Rheumatoid arthritis	Self reactive T lymphocyte	
Organ Transplantation		

Table 1